

We claim:

1. A soft capsule comprising

- (a) polymers prepared by polymerization of vinyl esters in the presence of polyethers
- (b) where appropriate structure-improving auxiliaries and
- (c) where appropriate other conventional constituents.

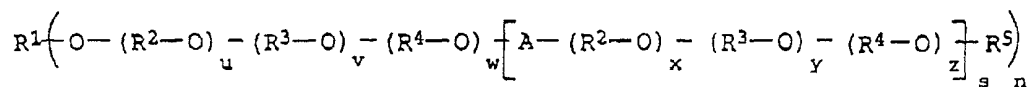
2. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of
- b) polyether-containing compounds and
- c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

3. A soft capsule as claimed in either of claims 1 or 2, wherein the polymers (a) are obtainable by free-radical polymerization of

- a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of
- b) polyether-containing compounds of the general formula I



We claim:

1. A soft capsule comprising

5

(a) polymers prepared by polymerization of vinyl esters in the presence of polyethers

(b) where appropriate structure-improving auxiliaries and

10

(c) where appropriate other conventional constituents.

2. A soft capsule as claimed in claim 1, wherein the polymers (a) are obtainable by free-radical polymerization of

15

a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of

b) polyether-containing compounds and

20

c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

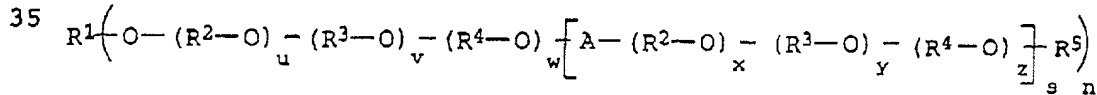
25

3. A soft capsule as claimed in either of claims 1 or 2, wherein the polymers (a) are obtainable by free-radical polymerization of

30

a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of

b) polyether-containing compounds of the general formula I



40

45

## 38

in which the variables have, independently of one another, the following meaning:

- 5       $R^1$     hydrogen,  $C_1$ - $C_{24}$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-, polyalcohol residue;
- 10       $R^5$     hydrogen,  $C_1$ - $C_{24}$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-;
- 10       $R^2$  to  $R^4$   
           $-(CH_2)_2-$ ,  $-(CH_2)_3-$ ,  $-(CH_2)_4-$ ,  $-CH_2-CH(R^6)-$ ,  
           $-CH_2-CHOR^7-CH_2-$ ;
- 15       $R^6$      $C_1$ - $C_{24}$ -alkyl;
- 15       $R^7$     hydrogen,  $C_1$ - $C_{24}$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-;
- 20      A     $-C(=O)-O$ ,  $-C(=O)-B-C(=O)-O$ ,  
           $-C(=O)-NH-B-NH-C(=O)-O$ ;
- 20      B     $-(CH_2)_t-$ , arylene, optionally substituted;
- 25      n    1 to 1000;
- 25      s    0 to 1000;
- 25      t    1 to 12;
- 30      u    1 to 5000;
- 30      v    0 to 5000;
- 30      w    0 to 5000;
- 35      x    0 to 5000;
- 35      y    0 to 5000;
- 40      z    0 to 5000;
- 40      and
- 45      c)    where appropriate one or more other copolymerizable monomers
- 45      and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

39

4. A soft capsule as claimed in any of claims 1 to 3, wherein the polymers (a) are obtainable by free-radical polymerization of

- 5 a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of
- b) polyether-containing compounds of the general formula I with a number average molecular weight of from 300 to 100000, in which the variables have, independently of one another, the following meaning:

R<sup>1</sup> hydrogen, C<sub>1</sub>-C<sub>12</sub>-alkyl, R<sup>6</sup>-C(=O)-, R<sup>6</sup>-NH-C(=O)-, polyalcohol residue;

R<sup>5</sup> hydrogen, C<sub>1</sub>-C<sub>12</sub>-alkyl, R<sup>6</sup>-C(=O)-, R<sup>6</sup>-NH-C(=O)-;

R<sup>2</sup> to R<sup>4</sup>  
-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>4</sub>-, -CH<sub>2</sub>-CH(R<sup>6</sup>)-,  
-CH<sub>2</sub>-CHOR<sup>7</sup>-CH<sub>2</sub>-;

R<sup>6</sup> C<sub>1</sub>-C<sub>12</sub>-alkyl;

R<sup>7</sup> hydrogen, C<sub>1</sub>-C<sub>12</sub>-alkyl, R<sup>6</sup>-C(=O)-, R<sup>6</sup>-NH-C(=O)-;

n 1 to 8;

s 0;

u 2 to 2000;

v 0 to 2000;

w 0 to 2000;

and

c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

## 40

5. A soft capsule as claimed in any of claims 1 to 4, wherein the polymers (a) are obtainable by free-radical polymerization of

5 a) at least one vinyl ester of  $C_1$ - $C_{24}$ -carboxylic acids in the presence of

10 b) polyether-containing compounds of the general formula I with a number average molecular weight of from 500 to 50000, in which the variables have, independently of one another, the following meaning:

$R^1$  hydrogen,  $C_1$ - $C_6$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-;

15  $R^5$  hydrogen,  $C_1$ - $C_6$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-;

$R^2$  to  $R^4$

- $(CH_2)_2$ -, - $(CH_2)_3$ -, - $(CH_2)_4$ -, - $CH_2$ -CH( $R^6$ )-,  
- $CH_2$ -CHOR<sup>7</sup>- $CH_2$ -;

20

$R^6$   $C_1$ - $C_6$ -alkyl;

$R^7$  hydrogen,  $C_1$ - $C_6$ -alkyl,  $R^6$ -C(=O)-,  $R^6$ -NH-C(=O)-;

25

n 1;

s 0;

u 5 to 1000;

30

v 0 to 1000;

w 0 to 1000;

35

and

c) where appropriate one or more other copolymerizable monomers

40 and subsequent at least partial hydrolysis of the ester functions in the original monomers a).

45

## 41

6. A soft capsule as claimed in any of claims 1 to 5, wherein the polymers (a) are obtainable by free-radical polymerization of

5 a) at least one vinyl ester of  $C_1$ - $C_{24}$ -carboxylic acids in the presence of

b) polyether-containing compounds and

10 c) where appropriate one or more other copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a), wherein the  
15 polyether-containing compounds b) have been prepared by polymerization of ethylenically unsaturated alkylene oxide-containing monomers and, where appropriate, other copolymerizable monomers.

20 7. A soft capsule as claimed in claim 6, wherein the polyether-containing compounds b) have been prepared by polymerization of polyalkylene oxide vinyl ethers and, where appropriate, other copolymerizable monomers.

25 8. A soft capsule as claimed in claim 6, wherein the polyether-containing compounds b) have been prepared by polymerization of polyalkylene oxide (meth)acrylates and, where appropriate, other copolymerizable monomers.

30 9. A soft capsule as claimed in any of claims 1 to 8, wherein the other copolymerizable monomer c) is selected from the group of:

35 acrylic acid, methacrylic acid, maleic acid, fumaric acid, crotonic acid, maleic anhydride and its monoesters, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, n-butyl acrylate, n-butyl methacrylate, t-butyl acrylate, t-butyl methacrylate, isobutyl acrylate, isobutyl methacrylate, 2-ethylhexyl acrylate, stearyl acrylate,  
40 stearyl methacrylate, N-t-butylacrylamide, N-octylacrylamide, 2-hydroxyethyl acrylate, hydroxypropyl acrylates, 2-hydroxyethyl methacrylate, hydroxypropyl methacrylates, alkylene glycol (meth)acrylates, styrene, unsaturated sulfonic acids such as, for example,  
45 acrylamidopropanesulfonic acid, vinylpyrrolidone, vinylcaprolactam, vinyl ethers (for example: methyl, ethyl, butyl or dodecyl vinyl ether), vinylformamide,

## 42

vinylmethyleacetamide, vinylamine, 1-vinylimidazole,  
1-vinyl-2-methylimidazole, N,N-dimethylaminomethyl  
methacrylate and N-[3-(dimethylamino)propyl]methacrylamide;  
3-methyl-1-vinylimidazolium chloride,  
5 3-methyl-1-vinylimidazolium methyl sulfate,  
N,N-dimethylaminoethyl methacrylate, N-[3-(dimethylamino)-  
propyl]methacrylamide quaternized with methyl chloride,  
methyl sulfate or diethyl sulfate.

10 10. A soft capsule as claimed in any of claims 1 to 9, wherein  
the ratios of amounts are

a) 10 to 98% by weight

15 b) 2 to 90% by weight

c) 0 to 50% by weight.

20 11. A soft capsule as claimed in any of claims 1 to 10, wherein  
the ratios of amounts are

a) 50 to 97% by weight

b) 3 to 50% by weight

25 c) 0 to 20% by weight.

30 12. A soft capsule as claimed in any of claims 1 to 11, wherein  
the ratios of amounts are

a) 65 to 97% by weight

b) 3 to 35% by weight

35 c) 0 to 20% by weight.

40 13. A soft capsule as claimed in any of claims 1 to 12, wherein  
the resulting polymers are subsequently crosslinked by a  
polymer-analogous reaction.

45 14. A soft capsule as claimed in any of claims 1 to 13, wherein  
dialdehydes, diketones, dicarboxylic acids, boric acid, boric  
acid salts, and salts of multiply charged cations are  
employed for the subsequent crosslinking.

## 43

15. A soft capsule as claimed in any of claims 1 to 14, wherein the structure-improving auxiliaries (b) employed are compounds from the following classes:

a) Polymers with a molecular weight of more than 50000

5

b) substances leading to crosslinking of the polymer chains of the polymers,

10

c) and, where appropriate, substances which lead to crosslinking of the polymer chains of the structure-improving auxiliaries.

16. A soft capsule as claimed in any of claims 1 to 15, wherein the structure-improving auxiliaries employed are polymers from the following classes of substances:

15

Polyamino acids such as gelatin, zein, soybean protein and derivatives thereof, polysaccharides such as starch, degraded starch, maltodextrins, carboxymethylstarch, cellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, carboxymethylcellulose, ethylcellulose, cellulose acetate, cellulose acetate phthalate, hydroxypropylcellulose acetate phthalate, hydroxypropylcellulose acetate succinate, hemicellulose, galactomannans, pectins, alginates, carrageenans, xanthan, gellan, dextran, curdlan, pullulan, gum arabic, chitin, and derivatives thereof, synthetic polymers such as polyacrylic acid, polymethacrylic acid, copolymers of acrylic esters and methacrylic esters, polyvinyl alcohols, polyvinyl acetate, polyethylene glycols, polyoxyethylene/polyoxypropylene block copolymers, polyvinylpyrrolidones and derivatives thereof.

20

25

30

17. A soft capsule as claimed in any of claims 1 to 16, wherein other conventional constituents of the shell which are present are fillers, release agents, flow aids, dyes, pigments, opacifiers, flavorings, sweeteners, plasticizers, preservatives and/or active ingredients.

35

18. A soft capsule as claimed in any of claims 1 to 17, wherein the shell consists of from 10 to 100% by weight of polymers of vinyl esters on polyether, where appropriate from 0 to 80% of structure-improving auxiliaries and, where appropriate, from 0 to 30% of other conventional constituents.

45



## 44

19. A soft capsule as claimed in any of claims 1 to 18, obtainable by processes such as the rotary die process, Accogel process, Norton process, drop or blow process or the Colton-Upjohn process.

5

20. A soft capsule as claimed in any of claims 1 to 19, which comprises one or more active pharmaceutical ingredients, vitamins, carotenoids, minerals, trace elements, food supplements, cosmetic active ingredients, crop protection agents, bath additives, perfume, flavoring, cleaner or detergent.

10

21. A soft capsule as claimed in any of claims 1 to 20, wherein the shell comprises from 20 to 80% of a polymer resistant to gastric fluid.

15

22. A soft capsule as claimed in any of claims 1 to 21, wherein resistance to gastric fluid is achieved by applying after production a coating resistant to gastric fluid by conventional pharmaceutical coating processes.

20

23. The use of the soft capsules as claimed in any of claims 1 to 22 for pharmaceutical applications.

25

24. The use of the soft capsules as claimed in any of claims 1 to 22 for cosmetic applications, applications in crop protection, for cleaners or food supplements.

30

25. The use of polymers obtainable by free-radical polymerization of

a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of

35

b) polyether-containing compounds and

c) where appropriate one or more copolymerizable monomers

40

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) to produce soft capsules as claimed in any of claims 1 to 22.

26. The use of polymers obtainable by free-radical polymerization of

45

Soft capsules comprising polymers of vinyl esters and polyethers,  
the use and production thereof

- 5 The present invention relates to soft capsules, for example for  
pharmaceutical applications, comprising polymers prepared by  
polymerization of vinyl esters in the presence of polyethers,  
and, where appropriate, in the presence of structure-improving  
auxiliaries and/or other conventional shell constituents, and to  
10 the use and production thereof.

- Soft capsules are distinguished by the fact that the production  
of the shell and the filling take place virtually simultaneously  
in one step. The shell of such capsules ordinarily consists  
15 mainly of gelatin, which is why the capsules are often also  
referred to as soft gelatin capsules. Since gelatin is per se a  
brittle material of low flexibility, it must be plasticized  
appropriately, i.e. plasticizers must be added. Such plasticizers  
are low molecular weight compounds, ordinarily liquids such as,  
20 for example, glycerol, propylene glycol, polyethylene glycol 400.  
Such capsules often additionally contain dyes, opacifying agents  
and preservatives.

- Although gelatin is frequently employed, it has numerous  
25 disadvantages. Thus, gelatin is a material of animal origin and  
thus not kosher. In addition, there is always a slight residual  
risk of BSE, because gelatin from cattle is preferably used to  
produce it. Obtaining suitable gelatin is very complicated and  
requires strict supervision of the process. Despite this,  
30 differences between batches are large because of the animal  
origin, which is subject to a certain variability. Gelatin is  
very susceptible to microbes because it represents a good  
nutrient medium for microorganisms. It is therefore necessary to  
take appropriate measures during the production as well as the  
35 use of such packaging materials. The use of preservatives is  
frequently indispensable.

- The plasticizers which are absolutely necessary to produce  
gelatin capsules frequently migrate from the shell into the  
40 filling and cause changes there. The shell loses plasticizers and  
becomes brittle and mechanically unstable during the course of  
storage. In addition, the shell of a soft gelatin capsule has a  
relatively high water content, which likewise has a plasticizing  
effect. On storage of such capsules with pure humidity there is  
45 evaporation of water from the shell, which likewise makes the  
capsule brittle. The same thing happens when very hygroscopic

45

a) at least one vinyl ester of C<sub>1</sub>-C<sub>24</sub>-carboxylic acids in the presence of

b) polyether-containing compounds and

c) where appropriate one or more copolymerizable monomers

and subsequent at least partial hydrolysis of the ester functions in the original monomers a) wherein the polyether-containing compounds b) have been prepared by polymerization of ethylenically unsaturated alkylene oxide-containing monomers and, where appropriate, other copolymerizable monomers, for producing soft capsules as claimed in any of claims 1 to 22.